REMARKS

In the present communication, claim 2 has been amended; claims 1, 5, 6, 8, 11, 12, 18 and 20-44 have been canceled; and no claims have been added. The amendments add no new matter and are fully supported by the specification and claims as filed. Upon entry of the present amendment, claims 2, 9, 10 and 19 will be pending in this application.

Rejections under 35 U.S.C §101

Applicants respectfully traverse the rejection of claims 2, 9-10 and 19 under 35 U.S.C. §102(b), as allegedly not supported by either a specific and substantial asserted utility or a well-established utility.

The Office Action acknowledges that numerous utilities are taught throughout the specification, however, the Office Action alleges that none of teachings with regard to the asserted utilities, indicate that that a nexus has been established between the glycosylation and a specific disease, disorder or physiological process, which one could reasonably predict to be affected by the administration of a compound identified by the claimed method. Further, the Office Action asserts that even if a specific utility were among those set forth in the specification, the identification and reasonable confirmation of a "real world" context of use for the screened compound would require further experimentation.

The proper test for determining whether an application complies with the utility requirement is set forth in M.P.E.P. §2107 which states that where the Applicant has "asserted that the claimed invention is useful for any particular practical purpose (i.e., it has a "specific and substantial utility") and the assertion would be considered credible by a person of ordinary skill in the art", a rejection based on lack of utility is improper. With regard to credibility, the credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record (*e.g.,* test data, affidavits or declarations from experts in the art, patents or printed publications) that is probative of the applicant's assertions. M.P.E.P. §2107. Further, an applicant need only provide one credible assertion of a specific and substantial utility for each claimed invention to satisfy the utility requirement. M.P.E.P. §2107.

Despite the numerous utilities acknowledged to be included in the application, Applicants submit herewith Maragakis et al. (*Arch Neurol*, 58:365-370 (2001)) which pertains to the role of glutamate transporters in neurologic disease. Specifically, Maragakis et al. implicate glutamate transporters, such as EAAT1, as potential causal factors in connection with neurologic diseases (pages 365-366). Applicants submit that based on the specification and the knowledge of one skilled in the art as evidenced in Maragakis et al., the asserted utility that neurological disorder may be affected by modulation of cellular glycosylation would be considered credible by one skilled in the art. A nexus is provided between glutamate transporters, such as EAAT1, and neurologic disease as discussed in Maragakis et al. Additionally, modulation of GTRAP3-18 expression or activity has been shown to modulate the activity of glutamate transporters, such as EAAT1, via glycosylation of such transporters (see Example 1). Applicants assert that one of skill in the art would consider that a credible assertion has been made that modulation of cellular glycosylation via modulation of GTRAP3-18 expression or activity may affect neurological disorder. The assertion that even if a specific utility were among those set forth in the specification, the identification and reasonable confirmation of a "real world" context of use for the screened compound would require further experimentation. Such an assertion is irrelevant as this is not the proper test in determining whether the utility requirement has been met.

Accordingly, the utility requirement has been met and reconsideration and withdrawal of the rejection is requested.

Rejections under 35 U.S.C §102

Applicants respectfully traverse the rejection of claims 2 and 19 under 35 U.S.C. §102(b), as allegedly anticipated by Lin et al. (*Nature*, 410: 84-88 (March 1, 2001)).

To anticipate, a single reference must inherently or expressly teach each and every element of the claimed invention. *In re Spada*, 15 USPQ2d 1655 (Fed Cir. 1990); and *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP § 2131.

The Office Action alleges, that Lin et al. teach each of the active steps of the claimed method including contacting a neuronal cell with a test compound and assaying the ability of the test

compound to modulate the expression of GTRAP3-18 protein expression. Specifically, the Office Action indicates that since claim 2 previously recited "assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide, or the activity of a GTRAP3-18 polypeptide" in the alternative, Lin et al., anticipates that claimed invention.

Without acquiescing to the rationale presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended claim 2 to recite a method for identifying a compound which modulates cellular glycosylation in which the test compound is identified by assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, thereby identifying a compound which modulates cellular glycosylation. Applicants assert that Lin et al. fail to teach a method including assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, nor does Lin et al. teach a method including assaying the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule. Since the reference fails to teach each and every element of the claims, the reference fails to anticipate the claimed invention.

Accordingly, withdrawal of the rejection under 35 U.S.C. §102(b) is respectfully requested.

Applicants respectfully traverse the rejection of claims 2 and 19 under 35 U.S.C. §102(e), as allegedly anticipated by U.S. Patent No. 6,808,893 (Rothstein et al.).

Specifically, the Office Action alleges, that Rothstein et al. teach methods comprising contacting cells with test compounds and assaying the ability of the test compounds to reduce GTRAP3-18 protein expression.

Without acquiescing to the rationale presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended claim 2 to recite a method for identifying a compound which modulates cellular glycosylation in which the test compound is identified by assaying the ability of the test compound to modulate the expression of a GTRAP3-18

nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, thereby identifying a compound which modulates cellular glycosylation. Applicants assert that Rothstein et al. fail to teach a method including assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, nor does Rothstein et al. teach a method including assaying the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule. Since the reference fails to teach each and every element of the claims, the reference fails to anticipate the claimed invention.

Accordingly, withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Rejections under 35 U.S.C §103(a)

Applicants respectfully traverse the rejection of claims 2, 9 and 10 under 35 U.S.C. §103(a), as allegedly obvious over Lin et al. as applied to claims 2 and 19, and further in view of Hirabayashi et al. (*Journal of Chromatography B*, 771: 67-87 (May 5, 2002)).

The recent U.S. Supreme Court decision in *KSR International v. Teleflex Inc.* (82 USPQ 2d 1385), modified the standard for establishing a *prima facie* case of obviousness. Under the *KSR* rule, three basic criteria are considered. First, some suggestion or motivation to modify a reference or to combine the teachings of multiple references still has to be shown. Second, the combination has to suggest a reasonable expectation of success. Third, the prior art reference or combination has to teach or suggest all of the recited claim limitations. Factors such as the general state of the art and common sense may be considered when determining the feasibility of modifying and/or combining references.

As discussed above, without acquiescing to the rationale presented in the Office Action, and in order to expedite prosecution of the instant application, Applicants have amended claim 2 to recite a method for identifying a compound which modulates cellular glycosylation in which the test compound is identified by assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a

GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, thereby identifying a compound which modulates cellular glycosylation.

Applicants submit that the Office Action fails to establish a *prima facie* case of obviousness because the cited references fail to provide some suggestion or motivation to modify a reference or combine the teachings of the reference to arrive at the claimed invention. As discussed above, Lin et al. fail to teach assaying the ability of the test compound to modulate the expression of a GTRAP3-18 nucleic acid molecule or polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule, or the activity of a GTRAP3-18 polypeptide by detecting the level of glycosylation of a GTRAP3-18 target molecule. The Office Action alleges that the active steps of the claim do not require a correlation between GTRAP3-18 expression and cellular glycosylation, but merely state that a compound identified as modulating GTRAP3-18 expression is thereby identified as a compound that modulates cellular glycosylation. However, Applicants note that the claims as amended require detecting the level of glycosylation of a GTRAP3-18 target molecule to identify the compound of cellular glycosylation. Lin et al. fail to teach or suggest a correlation between GTRAP3-18 activity regulation or expression and modulation of cellular glycosylation as claimed. The reference provides no suggestion or guidance as to a potential role of GTRAP3-18 in modulating cellular glycosylation and fails to provide any assay to determine the state of glycosylation of any GTRAP3-18 target molecules (*e.g.,* glutamate transporters, such as EAAT1), nor suggestion to undertake such an assay. Further, with specific regard to glutamate transporter EAAT1, the reference is silent with regard to EAAT1.

Likewise, Hirabayashi et al. also fail to remedy the deficiency since the reference fails to teach or suggest such a correlation. The Office Action alleges Hirabayashi et al. disclose a variety of techniques for quantification of protein glycosylation and that such methods are essential for understanding the effects of glycosylation which is involved in numerous biological phenomenon and that the skilled artisan would be motivated to combine the references to obtain a fuller investigation of cellular function. However, Hirabayashi et al. fail to teach or suggest identifying specific modulators of cellular glycosylation or any specific proteins involved in cellular glycosylation, such

as GTRAP3-18 or glutamate transporter EAAT1. Accordingly, one of skill in the art would not be motivated to determine glycosylation of proteins specifically in the GTRAP3-18 pathway, especially glutamate transporter EAAT1 which is not identified in either Lin et al. or Hirabayashi et al.

Applicants submit that even if one were to combine the teachings of Lin et al. and Hirabayashi et al., the resulting combination would not be *prima facie* obvious over the claimed invention since the combined teachings fail to disclose each and every claim limitation. As discussed above, Applicants respectfully submit that both Lin et al. and Hirabayashi et al. fail to provide a method of identifying a modulator of cellular glycosylation associated with the GTRAP3-18 glycosylation pathway as claimed. Further, Applicants respectfully submit that both Lin et al. and Hirabayashi et al. are silent with respect to the correlation between GTRAP3-18 activity regulation or expression and modulation of cellular glycosylation, as especially glutamate transporter EAAT1.

Accordingly, withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

The Commissioner is hereby authorized to charge the total amount of $555.00 to Deposit Account No. 07-1896 for payment of the Petition for Three-Month Extension of Time fee (small entity). No other fees are deemed necessary with the filing of this paper. However, if any additional fees are due, the Commissioner is further authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

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